AIDS
MEMORANDUM
Acquired Immune Deficiency Syndrome

National Institute of Allergy and Infectious Diseases

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IN THIS ISSUE

GROUND RULES FOR USE OF THE AIDS MEMORANDUM

The AIDS Memorandum serves as a forum for the rapid exchange of new information and ideas among clinicians and scientists involved in AIDS research and management. Material contained in the Memorandum can be of several kinds: positive and/or negative results, clinical and/or experimental findings, preliminary and/or validated data, observations, questions, theories, commentaries, and others. This material is not subjected to peer review. Therefore, users of the Memorandum must agree to treat all material as privileged information and to consider it as tentative and subject to change prior to formal publication in a refereed journal.

Users must agree not to cite material from the Memorandum without first obtaining the consent of the author(s), and, with author permission, to cite information only as a personal communication. Author addresses are provided for this purpose.

Users must agree to contribute data or ideas to the Memorandum at least once a year. On an annual basis, the names of individuals who have not contributed to the Memorandum will be culled from the mailing list, so as to limit circulation of the Memorandum only to individuals actively working in the field.

Finally, users must agree to share material in the Memorandum only with other individuals willing to honor these ground rules.

RESPONSES TO THE AIDS MEMORANDUM QUESTIONNAIRE

In late summer, a questionnaire (reprinted in the first issue of the AIDS Memorandum) was mailed to everyone whose name was on the Memorandum mailing list. About 60% of the questionnaires were completed and returned, and a number of thoughtful comments and suggestions were made. In general, respondents expressed a willingness to share observations, ideas, and experimental findings. Over 90% said they would be willing to contribute to future issues of the Memorandum.

Several respondents pointed out that the Memorandum could serve the purposes generally served by meetings and the grapevine, providing clinicians and researchers with opportunities to communicate easily and frequently, pose questions for each other, and benefit from each others' insights. This is clearly the intention of the Memorandum.

Many people wrote that they would find the Memorandum of use as it was defined in the cover letter accompanying the questionnaire. Many suggested additional and/or more specific ways in which the Memorandum could be of special value to them. Most respondents were unfamiliar with the Memorandum format and unaccustomed to sharing, in writing, preliminary ideas and data. Therefore, to help spark in Memorandum participants ideas about the kinds of information which might be shared through the Memorandum, some of the specific requests for information are described here.

In the area of patient care, a number of specific requests were made. Respondents wanted information describing newly recognized clinical associations, autopsy findings, comparisons of AIDS with similar conditions found in transplant recipients, newly defined laboratory abnormalities which might be closely associated with the disease, and disease manifestations in specific patient groups. In addition, respondents expressed interest in exchanging ideas about methods for screening patients and advising and informing them about AIDS, about any therapeutic advances and/or promising treatment protocols which may arise, and about new strategies for improving patient care.

Other comments concerned laboratory data. The feeling was widely held that the exchange of negative data would provide an important opportunity for workers in the field to avoid dead ends and to benefit from the experiences and mistakes of others. Several respondents pointed out that the provision of a general overview of the status of ongoing experiments would be invaluable, especially if a willingness to submit recent work were coupled with presentation of data in sufficient detail to permit peer review of the merits of the work. Respondents wanted technical exchanges of various kinds, such as information on how and where to store biopsy materials and blood samples. They also wanted data describing the results of experiments using animal model systems.

Several respondents anticipated that the Memorandum could be of value in helping them establish worthwhile collaborations. This could happen in two steps, first, through heightened awareness of work carried out by other groups and, second, through periodic publication of a list of Memorandum participants.

Many respondents commented on the importance of a rapid turnover time for new information and leads. One suggested that, at a minimum, the AIDS Memorandum

should precede newspapers in delivering the "news." One economy-minded respondent was pleased that the Memorandum was free.

Some concern was expressed that the ground rule requiring all participants to contribute information or ideas to the Memorandum annually would have two negative effects: it would make the Memorandum unavailable to those who might benefit from the information in it but might not be able to contribute to it, and it would encourage participants to send in "junk" in order to remain on the mailing list. The example cited in support of the former concern was of an ophthalmologist who saw only one or two AIDS patients a year. Such a clinician can contribute a single case report each year or, perhaps more importantly, an insight into or thought about some clinical feature of the syndrome. With regard to the second concern, although the Memorandum is not a journal, articles are reviewed and edited, in some cases heavily, by the scientific editorial staff of the Memorandum. The mandatory participation policy has worked for all other memoranda in the past and was adopted to encourage and to promote active involvement in the Memorandum by all active AIDS workers.

Any additional thoughts on and answers to the question "what would make the AIDS Memorandum a valuable resource for you?" would be welcome at any time. The AIDS Memorandum is a forum for the exchange of ideas and data about the many problems associated with this syndrome which, to date, has eluded all efforts at solution.

EXPERIMENTAL TRANSMISSION OF SIMIAN AIDS AND KAPOSI'S-LIKE SKIN LESIONS

A spontaneous disease which is similar to human AIDS has been found to occur in monkeys. Simian AIDS (SAIDS) was transmitted experimentally from two California rhesus monkeys dying of the disease to four NIH rhesus monkeys which, at the time of inoculation, were negative for cytomegalovirus (CMV) antibody. The inocula consisted of the supernatant fluid from 10% homogenates of various tissues with or without buffy coat cells from blood.

Recipient animals developed lymphadenopathy, splenomegaly, neutropenia, polymyositis, and other signs of the disease within a few weeks after inoculation. Two animals developed Kaposi's-like "patch" and "plaque" skin lesions, and one animal died with sepsis and profound lymphoid depletion. All animals became infected with CMV; however, antibody levels were low in two animals, appeared and then disappeared in one animal, and never developed in the one monkey which died.

This abstract describes data presented in an article which has been accepted for publication in The Lancet.

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SERUM PROFILES OF PNEUMOCYSTIS CARINII (PC) ANTIGENS AND ANTIBODIES IN AIDS PATIENTS

Serum profiles were determined for patients meeting the Centers for Disease Control criteria for AIDS and having biopsy diagnosed and/or clinically diagnosed Pneumocystis carinii pneumonia (PCP). PC antigenemia was measured by counterimmunoelectrophoresis (CIE) (Pifer LL, Hughes WT, Stagno S, et al: Pediatrics, 1978, 61:35-41; Pifer LL: Pediatr Infect Dis., 1983, 2:177-183). Anti-PC IgG titers were measured by an enzyme-linked immunosorbent assay (ELISA) (Pifer L, Niell H, Neely C, et al: Proc 19th Am Soc Clin Oncol., 1983, 2:abstract C-191).

Ten AIDS patients with PCP were tested for PC antigenemia. Of these 10, five had AIDS and Kaposi's sarcoma, one was a heroin addict, one was an infant with hemophilia, two had homosexual life styles as the only known risk factors, and one had no known risk factors. During their clinical courses with PCP, 9/10 (90%) exhibited PC antigenemia. None of 44 controls exhibited antigenemia; of these, 23 were volunteer blood donors from Memphis, Tennessee, and 21 were local, asymptomatic homosexual males.

In many cases of PCP, antigenemia appears in the subclinical or prodromal period. The results presented here suggest that the PC antigen test may prove useful as an early, noninvasive diagnostic test for PCP in AIDS patients.

Seventy-five percent of the AIDS patients referred for PC serology had anti-PC antibody (IgG) titers ranging from 1:128 to 1:512 by ELISA analysis. Over 75% of the healthy volunteer blood donors had titers of 1:256 or greater. In contrast, 76% of asymptomatic homosexual males had titers of 1:64 or less (Table).

ELISA IgG TITERS TO PC

PC IgG Titer	Asymptomatic Homosexual Males		AIDS Patients*		Healthy Volunteer Blood Donors	
	No.	(%)	No.	(%)	No.	(%)
1:16	17	(39)	2	(9)	0	(0)
1:32	17	(39)	3	(14)	4	(17)
1:64	10	(24)	3	(14)	2	(9)
1:128	14	(33)	6	(27)	3	(14)
1:256	1	(2.4)	7	(32)	3	(13)
1:512	1	(2.4)	5	(23)	14	(61)
1:1024+	0	(0)	2	(9)	3	(13)
	44		24		23	

* All of these sera were referred to our laboratory from other states for PC serologic profiles

It has been well documented that total IgG and IgA levels in AIDS patients are either within normal limits or elevated (Rogers MF, Morens DM, Stewart JA, et al: Ann Intern Med., 1983, 99:151-158). The preliminary data presented here show a difference in the specific humoral responses to PC in patients with AIDS and in asymptomatic homosexual males when compared with the responses in normal controls. AIDS patients have lower antibody titers than do normal controls, but their titers are not as low as those of the asymptomatic homosexuals. This suggests the possibility that some factor in the homosexual lifestyle is altering immune responsiveness. A reversal in the T helper/suppressor cell ratio has, for example, been established (Kornfield H, Van Stouwe RA, Lange M, et al: N Engl J Med., 1982, 307:729-731). Such a change may adversely affect the processing of PC antigens or may impair the natural process by which a normal antibody titer to PC is achieved and maintained. The finding of higher titers of anti-PC antibodies in AIDS patients as compared with asymptomatic homosexual controls is consistent

with the diagnosis of PCP in AIDS and with the clinical course of PCP which involves host humoral immune responses for resolving infection. Further investigations will be required to clarify the full significance of these preliminary findings.

Our laboratory will test specimens from AIDS patients for PC antigen and for antibody to PC. The tests will be performed without charge, although the sender must assume air freight charges. Please phone (901) 528-5942 or (901) 528-5932 for details.

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AN ANALYSIS OF *PNEUMOCYSTIS CARINII* PRE-MORTEM AND POST-MORTEM IN AIDS

Pneumocystis carinii pneumonia (PCP) is the most common clinical feature of AIDS, having been identified in 58% of patients to date (CDC Surveillance data). However, little has been written on the prevalence of *Pneumocystis carinii* (PC) in autopsy specimens of patients who die of AIDS (Masur H, Michelis MA, Greene JB: N Engl J Med., 1981, 308:1431-1438).

Forty-one AIDS patients were examined for evidence of PC organisms at autopsy, and many of these were also evaluated pre-mortem. The population consisted of 23 Haitians, 13 homosexual men, four intravenous drug abusers, and one hemophiliac. For all patients, at least one section of lung was stained with a Gomori-methenamine silver stain for PC, regardless of whether eosinophilic alveolar exudates were present or not.

PCP was diagnosed either pre-mortem, post-mortem, or both in 21 of the cases (51%). A pre-mortem diagnosis of PCP was made by identifying PC in lung tissues in 14 of the 41 cases (34%). Of these 14, PC could also be detected at autopsy in nine patients, and the cause of death was considered to be PCP in seven patients. The mean duration of clinical PCP from the time of tissue diagnosis to autopsy in the nine patients showing PC both pre-mortem and post-mortem was 20 days (range: 6 to 38 days). The therapy for PCP consisted of either trimethoprim and sulfamethoxazole or pentamidine; both of these may have toxic effects, especially in AIDS patients (Mitsuyasu R, Groopman J, Volberding P: N Engl J Med., 1983, 308: 1535). The therapy appeared to be effective in controlling PC in only those five patients in whom organisms were not seen at autopsy.

A post-mortem diagnosis of PCP was made by identifying PC in the autopsy specimens from 16 of the 41 cases (39%). Eleven of these patients had previously been shown to have PC pre-mortem. The cause of death in 11 patients was attributed to PCP; in seven of these, PC was detected during life while in four PC was detected only post-mortem. Death in two of the cases was considered to be caused by PCP, although disseminated cytomegalovirus infection could not be excluded with certainty. There were two additional cases for which PCP was not considered to be the primary cause of death, although PCP certainly was a significant secondary contributory cause of death. In another three cases positive at autopsy for PC but for which the cause of death was not PCP, only rare foci were present in the lungs and should not have been significant clinically.

The diagnosis of PCP in 51% of AIDS cases reported in this paper is similar to the national figure of 58%.

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CYCLOSPORIN IMMUNOSUPPRESSION AS THE POSSIBLE CAUSE OF AIDS

Many investigators have suggested that AIDS is caused by a transmissible infectious agent, most probably a virus (Curran J: N Engl J Med., 1983, 309:609-610). We propose that a non-viral infectious agent may act either as the primary causative agent of AIDS or as a secondary agent responsible for maintaining the disease state. Our hypothesis suggests that the severe impairment of the immune system and the subsequent fatal opportunistic infections in AIDS result from the systemic release of a potent cyclosporin-like immunosuppressive molecule from a fungal infectious agent.

Three different strains of the same fungal species have been isolated from long-term monocyte cultures of three AIDS patients. Simultaneous culture and examination of six normal human control monocyte cultures in the same culture plate showed no fungal growth or contamination. The fungal strains have been identified as atypical isolates of Thermoascus crustaceus (Dactylomyces crustaceus). Unlike the majority of soil or plant fungi, their optimum growth temperature is 37°C. Such fungi, including other species of Thermoascus, have never previously been isolated at the National Institutes of Health from either patients or normal individuals. They are unique isolates from clinical material from patients with AIDS.

The mycelia of these isolates contain a cyclosporin-like compound (CyAIDS) as detected by high-pressure liquid chromatography (HPLC) analyses. CyAIDS was found in high concentration near the reference peaks for cyclosporin A (CyA) and cyclosporin D standards (provided by Sandoz, Ltd). Mass spectrographic analyses of these samples are underway.

CyAIDS was also found in plasma samples studied by HPLC. Four out of four samples from patients with AIDS had CyAIDS peaks. The level of CyAIDS in the plasma of one patient was estimated to exceed 1,000 ng/ml. Two control blood samples failed to show significant levels of cyclosporin-like peaks. In contrast to these findings, no significant plasma cyclosporin levels could be measured in a radioimmunoassay for cyclosporin using a polyclonal sheep anticyclosporin antibody (provided by Sandoz, Ltd) (A. Palestine, personal communication). It is possible that CyAIDS produced by the fungi isolated from AIDS patients is sufficiently distinct immunologically that it cannot be detected by the sheep antibody. (Several different types of cyclosporins have been identified so far.) It is also possible that the AIDS patients produce antibodies against CyAIDS, and these could interfere with the radioimmunoassay.

The cyclosporins are hydrophobic, cyclical, neutral peptides containing 11 amino acids and having molecular weights of approximately 1,200 daltons (Wenger R: in White DJG (Ed): Cyclosporin A: Proc Int Conf CyA, Elsevier Biomed Press, 1982, 19-34). The CyA currently licensed by Sandoz for use in

transplantation (see below) is produced from a soil fungus strain originally classified as Trichoderma polysporum Rifai and now identified as Tolipocladium inflatum Gams (Borel J: in White DJG (Ed): Cyclosporin A: Proc Int Conf CyA, Elsevier Biomed Press, 1982, 5-17).

CyA is well known as a potent immunosuppressive substance. The mycelial extracts from Sabouraud broth cultures were observed to have an immunosuppressive effect in the mixed leukocyte culture assay. CyA has been shown to cause immunosuppression by inhibiting the production of interleukin-2 (IL-2) (Wagner H: Transplant Proc., 1983, 15:523-526) and by inhibiting the expression of IL-2 receptors on T helper cells (Palacios R, Moller G: Nature, 1981, 290:792-794). CyA also inhibits synthesis of gamma interferon (Reem G, Cook L, Vilcek J: Science, 1983, 221:63-65). When T cells are co-cultured with antigen or mitogen in the presence of CyA, they will not be transformed into activated cells. However, once a T cell expresses cytotoxic activity, it becomes resistant to the action of CyA. T suppressor functions are apparently not affected by CyA (Borel J: Transplant Proc., 1983, 15: 1881-1885).

Cyclosporin is used to induce immunosuppression following transplantation. Two to 13% of patients immunosuppressed in this way develop opportunistic infections and malignancies. In some cases, these effects may represent reactivation of Epstein-Barr virus (Sheil AGR: Transplant Proc., 1977, 9:1133-1138; Bird AG: in White DJG (Ed): Cyclosporin A: Proc Int Conf CyA, Elsevier Biomed Press, 1982, 307-315). One known effect of CyA therapy in man is the reversal of the T helper to T suppressor ratio through depletion of the number of T helper cells (Kerman RH, Van Buren CT, Flechner S, et al: Transplant Proc., 1983, 15:1971-1973). CyA therapy in dogs causes lassitude, fatigue, weight loss, diarrhea, and elevated globulin levels (Ryffel B: in White DJG (Ed): Cyclosporin A: Proc Int Conf CyA, Elsevier Biomed Press, 1982, 45-75).

Plasma from AIDS patients exerts an inhibitory effect on normal lymphocytes. It prevents such cells from responding to mitogens or to allogeneic lymphocytes (Cunningham-Rundles S, Michelis M, Masur H: J Clin Immunol., 1983, 3:156-165). An inhibitory factor in plasma from AIDS patients has been purified and has been shown to be a lov molecular weight compound. This compound impairs the production of IL-2 (G. Quinnan, personal communication). Typically, the T cells from AIDS patients fail to develop IL-2 receptors (J. Fahey, personal communication). In vitro, IL-2 can restore the cytotoxic response of lymphocytes from AIDS patients (Rook A, Masur H, Lane C, et al: J Clin Invest., 1983, 72:1-6).

The isolates of T. crustaceus were obtained from monocyte cultures. It seems unlikely that monocytes are the primary targets of infection in AIDS patients. However, if the fungi can grow in monocytes, their transmission would be possible from one individual to another through a needle stick or through blood components.

These results are extremely preliminary. The fungi may simply be contaminants of the monocyte cultures or opportunistic infectious agents in the AIDS patients. More isolations are needed. Further studies of the CyAIDS compounds isolated from both blood from patients with AIDS and mycelia of the fungus will be needed to determine whether the immunosuppressive activity will have any consequence in vivo. The fungus and the CyAIDS may simply be cofactors which,

along with other infectious agents, are necessary for inducing the full impairment of the immune system characteristic of AIDS. However, the types of immunologic impairments typical of AIDS and many of the immunosuppressive activities produced by the cyclosporins are comparable and would be consistent with an active role for a cyclosporin-like molecule in the immune suppression characteristic of AIDS.

This fungus may not prove on further evaluation to be the etiologic agent of AIDS. It is important, however, to consider a wide range of infections and infectious agents which might be responsible for the immunodeficiencies seen in the AIDS patients. It is also important to consider etiologic factors other than infectious agents as possible cofactors or initiators of AIDS.

This article includes information contained also in a letter which has been accepted for publication in the New England Journal of Medicine.

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HISTOLOGIC OBSERVATIONS IN AIDS AND KAPOSI'S SARCOMA (KS)

An etiologic role for bacteria has not been systematically explored in AIDS and KS. This report describes histologic observations made on biopsy materials from a 29-year-old white homosexual man with AIDS and KS. Permission for autopsy could not be obtained in this case.

A lymph node showing reactive hyperplasia was excised and examined with a Fite stain 2 months before the patient's death. Intracellular, purple coccoid forms and large Russell bodies were seen within a stained, acid-fast section of the node. The Russell bodies appeared to develop from the coccoid forms. Staphylococcus epidermidis was cultured from the node. Similar structures were seen in the surrounding connective tissue. Intracellular coccoid forms were seen within liver cells in liver biopsy sections characterized as showing nonspecific inflammation.

The patient developed multiple KS skin lesions on his face 2 weeks before death. Both intracellular and extracellular purple coccoid forms (Fite stain) and very rare pink coccoid forms (Gram stain) were observed throughout the dermis. These coccoid forms resembled some of the coccal forms of beta-Streptococcus, group G, which were isolated from a blood culture obtained 1 day before death. Some aberrant "large forms" of streptococci were similar in size to some of the Russell bodies observed in vivo within the lymph nodes.

The histopathological finding of coccoid forms in vivo in AIDS and KS is not a syndrome-specific finding. Similar structures have been observed in forms of cancer, collagen diseases, lymphoproliferative diseases, and in "normal" tissue (Cantwell AR, Jr: in Domingue GJ (Ed): Cell Wall Deficient Bacteria: Basic Principles and Clinical Significance. Addison-Wesley Publishing Company, Reading, Massachusetts, 1982, 321-360). However, other studies from this and other laboratories have also shown intracellular and extracellular coccoid forms associated with AIDS and KS. They have

been seen within enlarged lymph nodes of one suspected AIDS patient and within the skin lesions in two homosexual men with AIDS (Cantwell AR, Jr: Growth, 1982, 46:331-336; Cantwell AR, Jr: Cutis, 1983, 32:58-64, 68). Cell wall deficient bacteria (CWDB) have been detected in necroscopic analyses of sections of the heart, lungs, intestines, and in KS skin lesions of a 74-year-old Jewish man who died without clinical evidence of ante-mortem infection. Various bacteria--Corynebacterium sp. and Propionibacterium acnes from one case and Staphylococcus epidermidis and Streptococcus viridans from another--were cultured from the skin lesions of two of three elderly, heterosexual Jewish men with KS (Cantwell AR, Jr: Growth, 1981, 45:79-89). In eight of nine patients with AIDS and KS, acid-fast Mycobacterium avium-intracellulare have been detected at autopsy (Zakowski P, Fligiel S, Berlin GW, et al: J Am Med Assoc., 1982, 248:2980-2982). The Russell bodies and other bacterial forms seen in in vivo sections might be related to cell wall deficient and acid-fast forms of staphylococci, streptococci, and corynebacteria-like organisms which have been observed and cultured from samples of blood of both healthy and diseased individuals (Wuerthele-Caspe Livingston V, Livingston AM: Trans NY Acad Sci., 1972, 34:433-453).

Further studies are necessary to establish a link between histologic observations and clinical isolates. "Occult" bacteria were finally determined to cause "legionnaires' disease"; they may, likewise, prove to have more than an opportunistic role in AIDS.

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AIDS FROM CENTRAL AFRICA IN A HETEROSEXUAL DANISH MALE

The second Danish patient with AIDS of probable African origin recently died in Copenhagen at age 31. He was a previously healthy businessman who moved to central Africa in 1974. From 1974 to 1976 he lived mostly in Rwanda and from 1976 to 1980 in neighboring Burundi. During this time he paid short visits to Kenya; he also spent 2 days in Zaire. Between 1979 and 1981 he visited the Ivory Coast for 1 month and Canada for 1 week (crossing briefly into the United States). In December 1981 he left Burundi. From then until his death, he lived in France, the Ivory Coast, and Denmark.

The patient had never received a blood transfusion, and he denied homosexuality and intravenous drug abuse.

While in Rwanda in 1974, he contracted infectious mononucleosis. The diagnosis was confirmed in Denmark. In 1976 he developed bilateral orchitis of unknown origin. He was treated for gonorrhoea on several occasions in Burundi and for syphilis once in France after his last visit to Burundi. The venereal diseases were probably acquired from native (Watutsi) bar girls in Bujumbura, the capital of Burundi.

The patient was slightly obese but otherwise in good health until his return to Europe from Burundi in January 1982. He developed fatigue and fever and possibly lymphadenopathy. He was treated for toxoplasmosis in France, but a firm diagnosis was never established; and serological tests performed in 1983 for toxoplasmosis were negative. He had episodes of fever, and his general level of health gradually deteriorated. In November 1982, while taking antimalarials for fever, a long-lasting skin

eruption appeared. He was hospitalized in December of that year with a bleeding nose.

The patient suffered from functional dyspnoea and weight loss during 1983. He was examined for malaria because of recurrent fever. Malaria was not confirmed. By August of that year, he had lost 25 kg and was dyspnoeic even when at rest.

On August 12 he was rehospitalized. He required artificial respiration, as the initial discrete bilateral pulmonary infiltrates rapidly progressed despite high-dose erythromycin, sulfamethoxazol-trimethoprim, and prednisone therapies. An open lung biopsy revealed Pneumocystis carinii (PC) and cytomegalovirus (CMV) infections. Pentamidine and acyclovir therapies were started, but pneumothorax, progressive respiratory insufficiency, and later hypotension with anuria supervened. He died on August 31. An autopsy was not performed.

Lymphocyte counts of cells in peripheral blood showed severe lymphopenia ($0.14 \times 10^9/l$). No proliferative responses could be measured to mitogens and antigens in vitro. The T helper/T suppressor ratio was low (0.09), and NK cell activity was moderately decreased. (Lymphocyte studies were performed by the Tissue Type Laboratory, Rigshospitalet.) The S-IgA level was above normal; IgG and IgM levels were normal. Antinuclear antibodies and lymphocytotoxic antibodies were not found. The anti-CMV antibody titer was positive (1:128) as was the Epstein-Barr IgG antibody titer.

The patient fulfills the AIDS criteria but does not fit into any of the risk groups defined to date. We suggest that "Africans" be included in the list of risk groups. In addition, since this patient is suspected of having acquired his immune deficiency syndrome from heterosexual contact with Africans, we suggest that such contact would constitute another risk factor for AIDS.

In certain central African countries Kaposi's sarcoma (KS) is common. The highest prevalence of KS--about 12% of all cancers--is found in Zaire (Hutt MSR: Antibiot Chemother., 1981, 29:3-8).

The first case of an AIDS-like disease of probable African origin occurred in 1976 in a 46-year-old Danish woman surgeon who had been working in Zaire. She died of PC pneumonia in 1977 (Bygbjerg IC: Lancet, 1983, 1:925). Reports from Belgium (Clumeck N, Mascart-Lemone F, de Maubeuge J, et al: Lancet, 1983, 1:642) and France (Brunet JB, Bouvet E, Chaperon J, et al: Lancet, 1983, 1:700-701) point to Zaire and Chad as risk areas for AIDS. Next to Zaire, Burundi has the highest prevalence of African KS (Hutt, 1981). Other cases of AIDS are expected to develop in African immigrants to Europe and among Europeans who visit or live in Africa. Cases probably have occurred but may simply have been overlooked in the past. The case of AIDS described in this report reinforces the connection between KS and AIDS in the central African area.

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A PERSPECTIVE ON AIDS CASES AMONG HEALTH CARE WORKERS

It has been common knowledge at least since early 1982 that the epidemiology of AIDS is similar in many ways to that of hepatitis B. As a result, the

possibility that the disease might be transmitted to health care workers or laboratory staff handling materials from AIDS patients has been a constant concern. Formal recommendations for the protection of clinical and laboratory workers were drawn up by consensus among USPHS agencies and published in November, 1982 (Morb Mort Weekly Rep., 1983, 31:577-580). In mid-July, 1983, the Centers for Disease Control (CDC) published abstracts of four cases of AIDS among health workers who did not appear to belong to any of the recognized high-risk groups (Morb Mort Weekly Rep., 1983, 32:358-360). Although the editor concluded that "these four cases provide no new information regarding occupational risk related to health care personnel," the anecdotal reports have heightened the level of anxiety among persons whose responsibilities include caring for AIDS patients or analyzing biological specimens derived from them.

Before one attempts to consider the significance of the observation of four AIDS cases among medical personnel, it is necessary to estimate how many cases might have been expected merely on the basis of chance. In mid-July, 1983, the total number of AIDS cases that had been reported to CDC was 1902, of whom 110 could not be assigned to any of the designated high-risk groups. The four health workers were among this group of 110. According to the 1980 census, the United States population in the age brackets 18-64 totaled 137.2 million (US Bureau of the Census, Statistical Abstract of the United States, 1982-1983, 103rd ed, Washington, DC, 1982, xviii). This age span encompasses almost all employed persons and virtually all AIDS cases. The National Center for Health Statistics (NCHS) reports that in 1980 there were approximately 7.23 million persons employed in the health industry (NCHS: Health, United States, 1982, DHHS Publication No. (PHS) 83-1232, Table 51, 112). If, then, employment in the health industry bears no relationship to risk of AIDS, the number of health workers that would be expected among the 110 "unexplained" cases = $110 \times 7.23/137.2 = 5.8$, which exceeds the four observed. No elaborate statistical analysis is required to realize that this comparison does not support a hypothesis that health workers are at increased risk for the acquisition of AIDS. On the other hand, neither does it argue for cavalier disregard of common-sense precautions.

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SAFETY PRECAUTIONS FOR PERFORMING LABORATORY TESTS ON SPECIMENS FROM KNOWN OR SUSPECTED AIDS PATIENTS

The safety precautions advised for personnel involved with AIDS research were published in Morbidity and Mortality Weekly Reports in November 1982. The precautions specific to personnel performing laboratory tests or studies on clinical specimens or other potentially infectious materials from known or suspected AIDS cases are reprinted here. The precautions recommended for personnel handling experimental animals were reprinted in the first issue of the AIDS Memorandum, and other precautions will be reprinted in future issues.

- Mechanical pipetting devices should be used for the manipulation of all liquids handled in the laboratory. No mouth pipetting should be allowed.
- Needles should not be bent after use. They should be placed in a puncture-resistant container used only for

their disposal. They should not be reinserted into their original sheaths, since this process frequently is the cause of needle-associated injuries.

• Disposable syringes and needles should be used. Only needle-locking syringes or one-piece needle-syringe units should be used to aspirate fluids from patients, so that subsequent discharge of the fluid can be performed safely. If reusable syringes must be used, they should be decontaminated before reprocessing.

• Laboratory coats, gowns, or uniforms should be worn while work with potentially infectious materials is being done, and they should be discarded appropriately before leaving the laboratory.

• Gloves should be worn to avoid skin contact with the following: blood, specimens containing blood, blood-soiled items, body fluids, excretions, secretions, and surfaces, materials, and objects exposed to these specimens.

• All procedures and manipulations of potentially infectious materials should be performed carefully to minimize the creation of droplets and aerosols.

• Biological safety cabinets and other primary containment devices (e.g., centrifuge safety cups) should be used whenever procedures are conducted that are likely to create aerosols or infectious droplets. Such procedures include centrifuging, blending, sonicating, vigorous mixing, and harvesting infected tissues from animals or embryonated eggs. Fluorescence activated cell sorters also generate droplets that might form infectious aerosols. Translucent plastic shielding between the droplet-collecting area and the equipment operator should be used. Primary containment devices should be used for handling materials that might contain infectious agents or organisms in higher concentrations than expected in clinical specimens.

• Laboratory work surfaces should be decontaminated following any spill of potentially infectious material and at the completion of work activities. A disinfectant, such as sodium hypochlorite solution (a 1:10 dilution of 5.25% sodium hypochlorite [household bleach] with water), should be used.

• All potentially contaminated materials used in laboratory tests should be decontaminated, preferably by autoclaving, before disposal or reprocessing.

• All personnel should wash their hands following completion of laboratory activities, removal of protective clothing, and before leaving the laboratory.

NATIONAL AIDS/PRE-AIDS EPIDEMIOLOGICAL NETWORK (NAPEN)

In August 1983, NAPEN was officially formed. The idea for the network arose out of a suggestion to the CDC's AIDS Task Force that active surveillance of AIDS and sexually transmitted diseases common in homosexual populations should be initiated. A time course for disease progression was envisioned. Communities showing different incidence rates for AIDS were considered to be at unlike points along the time line; some communities would be at the point of introduction of the etiologic agent(s) into the community, others would be at the point of saturation with the agent(s), and others would be at the point of maximum occurrence of disease. Through a prospective study carried out simultaneously in several homosexual male communities with differing AIDS incidence rates, useful information could be

gained which might clarify the natural history and the etiology of AIDS.

The objectives of NAPEN have been formulated to include the following. The organization will serve as a forum for the exchange of ideas, methodologies, and information among epidemiological investigators. It is anticipated that such exchanges will result in adoption of standardized core epidemiological data bases and methodologies. A uniform data base will be developed for studying national trends and major risk and protective factors. Uniform reporting and data collecting instruments and procedures will be developed in conjunction with and distributed to investigators throughout the U.S. and Canada.

Anyone interested in joining NAPEN or in receiving further information should contact Laura Coats, Howard Brown Memorial Clinic, 2676 N. Halsted Street, Chicago, Illinois 60614, (312) 871-5777.

The requirements established for voting members are active involvement in AIDS epidemiologic research (including adherence to the confidentiality provisions of the Federation of AIDS Organizations), willingness to contribute data to NAPEN, and an initial membership fee of $10. Non-voting observers (administrators, funding agencies, and the like interested in furthering AIDS epidemiological investigations) and consultants (those performing a particular task and/or lending expertise) are also welcome. To date, there are 24 voting members in 19 cities, 30 observers, and three consultants.

D. G. Ostrow, Director of Research, Howard Brown Memorial Clinic, Associate Professor of Psychiatry and Community Health/Preventive Medicine, Northwestern University Medical School, Chicago, Illinois 60614.

UPCOMING AIDS MEETINGS

Registration is still open for the following upcoming AIDS meetings.

NAPEN Meeting (held in conjunction with the Annual Meeting of the American Assoc. of Public Health)
November 13, 1983
Dallas Hyatt Regency
Dallas, Texas

Contact:
Laura Coats
Howard Brown Memorial Clinic
2676 N. Halsted Street
Chicago, IL 60614
(312) 871-5777

UCLA Symposium: AIDS
February 5-10, 1984
Park City, Utah

Program Information:
Dr. Michael S. Gottlieb
103 Molecular Biology Institute
University of California
Los Angeles, CA 90024
(213) 206-6292
Registration Information:
Deadline for applications is November 1, 1983.

NAPEN Meeting (held in conjunction with the joint annual meeting of AAPHR and the National Coalition of Gay STD Services)
April 25-29, 1984
New Orleans, Louisiana

Contact:
Laura Coats
Howard Brown Memorial Clinic
2676 N. Halsted Street
Chicago, IL 60614
(312) 871-5777

AIDS CASES REPORTED TO THE CENTERS FOR DISEASE CONTROL AS OF OCTOBER 19, 1983

UNITED STATES CASES

DISEASE	CASES	PERCENT OF TOTAL	DEATHS	PERCENT DEAD
KS without PCP	665	26.5	146	21.9
PCP without KS	1282	51.0	599	46.7
Both KS and PCP	180	7.2	107	59.4
OI without KS or PCP	386	15.3	196	50.8
TOTAL	2513	100.0	1048	41.7

KS = Kaposi's sarcoma PCP = Pneumocystis carinii pneumonia
OI = Opportunistic infections

	MALES		FEMALES		TOTAL	
RISK GROUPS*	CASES	% OF TOTAL	CASES	% OF TOTAL	CASES	%
Homosexual or bisexual	1805	76.9	0	0.0	1805	71.8
IV drug user	337	14.4	87	52.7	424	16.9
Haitian	102	4.3	15	9.1	117	4.7
Hemophiliac	16	0.7	0	0.0	16	0.6
No apparent risk group or unknown	87	3.7	63	38.2	151	6.0
TOTAL	2347	100.0	165	100.0	2513	100.0

* The risk groups listed are hierarchically ordered; cases with multiple risk factors are tabulated only in the risk group listed first.

CASES REPORTED FROM OTHER COUNTRIES

NUMBER OF COUNTRIES	CASES
21	156

U.S. AND FOREIGN CASES REPORTED

TOTAL	2669